

## SCIENTIFIC ABSTRACT

One appealing approach to the treatment of late stage neuroblastoma uses an immunotherapy based strategy. Studies using animal models of different tumors have shown that gene modified tumor cells expressing a variety of cytokines are often made highly immunogenic. These tumor cells frequently demonstrate delayed growth and even outright rejection in vivo. A Phase I trial of vaccination with genetically modified Interleukin-2 secreting allogeneic neuroblastoma cells has just been completed here at St. Jude Children's Research Hospital. The trial demonstrated both the safety and potential therapeutic utility for this strategy. No significant complications were observed, and cell mediated cytotoxicity towards the allogeneic neuroblastoma cells were detected. One patient had evidence of tumor regression at distal sites, and six patients had stable disease for up to one year. Although these results are encouraging, this particular strategy has not been effective at eliminating large established tumors.

Experimental data have suggested, however, that combinations of cytokines may act synergistically to effect a stronger immune response. This might then enable the host to reject established tumors and have immunologic memory. One cytokine which appears to be complementary to IL2 is lymphotactin. Lymphotactin acts as an attractant for lymphocytes. Co-expression of this chemoattractant cytokine with interleukin-2 in an in vivo murine leukemia model afforded protection from the growth of established tumors as well as showing significant chemo- attraction for helper T-lymphocytes to the site of inoculation.

The goals of this project are to determine whether this combination of cytokines when expressed by allogeneic tumor cells can be given safely and might enable a host to reject established tumors and have immunologic memory.